REMARKS

Pending Claims

Applicants note the allowance of claims 54-60. The present amendment cancels claims 42, 44, 46-50 and 53-62 without prejudice to or disclaimer of the subject matter contained therein. Applicants reserve the right to file an application directed to the subject matter of the canceled claims pursuant to 35 U.S.C. § 120. The remaining claims are amended to incorporate base claims into dependent claims found otherwise allowable and to retain dependencies upon pending claims.

Lineage of the Application

The Examiner indicates that the present application is being considered as a Continuation-In-Part application. This appears to be due to the recitation in claim 44 that the helper cells might comprise a Venezuelan Equine Encephalitis virus replicon and helper RNAs. Applicants were invited to amend the specification to recite that the present application is a CIP application.

Applicants have canceled claim 44, thus no amendment of the specification is needed.

Rejection over Johnston

Claim 44 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Johnston et al. '462. Claim 44 is canceled, rendering this rejection moot.

Double Patenting Rejections

Claims 42, 46-50, 61 and 62 stand rejected under the judicially-created doctrine of obviousness-type double patenting over claims 13, 18, 24, 33, 37, 39 and 40-43 of U.S. Patent 5,739,026 and over claims 28 and 45-50 of U.S. Patent 6,190,666. These rejections are rendered moot in view of the cancellation of these claims. Applicants, however, still maintain their position that the rejection over the '026 patent was improperly drawn in including claims 13 and 18 of the '026 patent. The Examiner takes a position that a cell harboring the replicon nucleic acid is non-functional without also harboring at least one helper vector. Applicants note that cells harboring only replicon nucleic acids have utility in producing desired protein products *in vitro*. Thus the cells of claims 13 and 18 of the '026 patent are useful even if they do not harbor any helper vector.

Rejections under 35 U.S.C. § 112, first paragraph

Claim 53 stands rejected under 35 U.S.C. § 112, first paragraph, for alleged failure of the specification (1) to provide adequate

written description of a generic vaccine and (2) to enable practice of the claimed invention. Claim 53 has been canceled, rendering these rejections moot.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 53 and 63 are rejected under 35 U.S.C. § 112, second paragraph for failure of the claims to adequately define the subject matter of the invention. Claim 53 is canceled, rendering that rejection moot.

As to claim 63, the Examiner indicates that the language of the claim leaves open the possibility that some helper vector in the system might contain a packaging signal. Claim 63 is amended in a manner to clarify that each helper vector employed lacks a packaging signal.

Applicants submit that the present claims are directed to patentable subject matter and that the specification well-describes the claimed invention. The favorable action of allowance of the application is respectfully requested.

If there are any minor matters precluding allowance of the application, which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. (Reg. No. 36,623) at (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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By _____

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Attachments: Mark-up Version Showing Changes
Abstract

MARK-UP VERSION SHOWING CHANGES

In the Abstract of the Disclosure:

The following Abstract of the Disclosure was added to the application:

--Abstract of the Disclosure

The disclosure describes recombinant alphavirus RNA molecules and expression of heterologous proteins therefrom in animal cells. Recombinant alphaviruses of the present invention, when made to express an antigenic protein, can be administered as vaccines.--

In the Claims:

43. (Amended) [The helper cell according to claim 42,] A helper cell for producing an infectious, defective alphavirus particle, comprising, in an alphavirus-permissive cell:

(a) an alphavirus replicon RNA, wherein the alphavirus is selected from the group consisting of Sindbis virus and Semliki Forest virus; wherein the replicon RNA comprises the alphavirus packaging signal, a heterologous RNA sequence, and a sequence encoding at least one of the alphavirus structural proteins, wherein the replicon RNA furthermore lacks a sequence encoding at least one of the alphavirus structural proteins; and

(b) at least one separate helper RNA encoding the structural protein(s) absent from the replicon RNA, said helper RNA(s) lacking the alphavirus packaging signal;

wherein the combined expression of the replicon RNA and the helper RNA(s) produces an assembled alphavirus particle which comprises a heterologous RNA sequence, is able to infect a cell, and is unable to complete viral replication in the absence of helper RNA due to the absence of the structural protein coding sequence in the packaged replicon, wherein said replicon RNA encodes the alphavirus capsid protein, and wherein said at least one separate helper RNA(s) encodes the alphavirus E1 glycoprotein and the alphavirus E2 glycoprotein.

51. (Amended) [The method according to claim 50] A method of making infectious, defective, alphavirus particles, comprising:

providing a helper cell according to claim 43;

producing said alphavirus particles in said helper cell; and

collecting said alphavirus particles from said cell, wherein said alphavirus replicon RNA and said at least one separate helper RNA are introduced into said helper cell by electroporation.

52. (Amended) Infectious alphavirus particles produced by the method of claim [50] 51.

63. (Amended) A helper cell for producing an infectious, defective alphavirus particle, comprising, in an alphavirus-permissive cell:

(a) an alphavirus replicon RNA, wherein the alphavirus is selected from the group consisting of Sindbis virus and Semliki Forest virus; wherein the replicon RNA comprises the alphavirus packaging signal, a heterologous RNA sequence, and a sequence encoding at least one of the alphavirus structural proteins, wherein the replicon RNA furthermore lacks a sequence encoding at least one of the alphavirus structural proteins; and

(b) a helper RNA system comprising helper RNAs encoding the structural protein(s) whose transcripts are absent from or otherwise not functional in the replicon RNA, each of said helper RNA(s) lacking any alphavirus packaging signal;

wherein the combined expression of the replicon RNA and the helper RNA(s) produces an assembled alphavirus particle which comprises a heterologous RNA sequence, is able to infect a cell, and is unable to complete viral replication in the absence of helper RNA

due to the absence of at least one structural protein coding sequence in the packaged replicon.